

Amendments to the Drawings:

The attached sheets of drawings include changes to Figures 3-5. These sheets, which include Figures 3-5, replace the replacement sheets of drawings, submitted with the Amendment dated August 22, 2003, including Figures 3-5. In Figures 3-5, the term "BF100" has been deleted and replaced with the term "NRRL B-11474".

Attachment: Replacement Sheets (3)
Annotated Sheets Showing Changes (3)

REMARKS/ARGUMENTS

Claims 1-2 and 19 have been amended by this Amendment. Claims 21-23 have been cancelled by this Amendment. Claim 4 has been previously cancelled, and claims 9-11 and 14-18 have been previously withdrawn. Claims 1-3, 5-8, 12-13 and 19-20 are currently pending in the application, stand rejected, and are at issue.

Allowable Subject Matter

In the Final Office Action, the Examiner has objected to claim 3 as being dependent upon a rejected base claim, but has indicated that claim 3 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. However, Applicant does not deem it necessary to rewrite claim 3 in independent form. Applicant has amended the specification to include a description of what Deposit Number NRRL B-30293 contains and, accordingly, believes that such amendment places claim 2 in allowable form. Claim 3 depends from claim 2, and is also believed allowable.

Objections to Drawings

In the Final Office Action, The Examiner has objected to the description of figures on page 4 of the application. Specifically, in the description of Figure 2, the Examiner indicates that there is no sequence identifier of the wild-type pyruvate carboxylase. Additionally, the Examiner submits that the description of Figures 3-5 refer to "*C. glutamicum* NRRL B-11474" while the figures show "BF100". In the Advisory Action, the Examiner indicated that there is no evidence that the strain "BF100" is the same strain as "NRRL B-11474" and not "NRRL B-30293".

In response, Applicant has amended the description of Figure 2 in accordance with the Examiner's suggested description. With respect to Figures 3-5, while "BF100" has been

designated as "NRRL B-11474" by Applicant such that the two may be used interchangeably, Applicant has amended Figures 3-5 to refer to "*C. glutamicum* NRRL B-11474" so that the description of Figures 3-5 matches said figures.

Applicant submits that the specification is clear that the strain "BF-100" is the same strain isolated from "NRRL B-11474". The description with respect to Figures 3-5 is clear that Applicant is comparing the pyruvate carboxylase strain isolated and cloned from "NRRL B-11474" with the strain found in "ATCC 21253". Moreover, Applicant has previously amended Table 2 to remove the reference to "BF100" and has replaced it with "NRRL B-11474". While the pyruvate carboxylase gene isolated and cloned from "NRRL B-11474" was deposited in an *E. coli* host cell under deposit "NRRL B-30293", it is the strain from "NRRL B-11474" that was analyzed and compared with the strain found in "ATCC 21253". The specification is clear on this point, and Applicant respectfully requests that the drawing correction as well as correction to the specification be approved.

Objections to Sequence Listing

In the Final Office Action, the Examiner has objected to the current Sequence Listing, filed August 22, 2003.¹ The Examiner alleges that the Sequence Listing fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825. Applicant respectfully traverses the Examiner's objections for at least the following reasons.

Section 1.821(c) states, in pertinent part:

The sequence identifiers must begin with 1 and increase sequentially by integers.
If no sequence is present for a sequence identifier, the code "000" must be used in

¹ In the Advisory Action, the Examiner indicated that Applicant's arguments were persuasive with respect to the Sequence Listing. However, said arguments are reproduced herein in view of the requested non-entry of the previously filed Amendment.

place of the sequence. The response for the numeric identifier <160> must include the total number of SEQ ID NOs, whether followed by a sequence or by the code "000."

37 CFR § 1.821(c). The substitute Sequence Listing filed August 22, 2003 complies with these requirements. SEQ ID NOs:3 and 4 have been deleted by the Amendment filed August 22, 2003. The substitute Sequence Listing was amended to reflect this deletion by using the code "000" in place of the sequences for deleted SEQ ID NOs:3 and 4, in accordance with the sequence disclosure requirements. Additionally, the numeric identifier <160> includes the total number of SEQ ID NOs, namely 19, which includes the total number of sequence identifiers followed by a sequence or by the code "000", in accordance with the sequence disclosure requirements. Accordingly, Applicant respectfully submits that the substitute Sequence Listing filed August 22, 2003 complies with the sequence disclosure requirements, and respectfully respects withdrawal of the Examiner's objection to the Sequence Listing.

Objections to Specification

In the Final Office Action, the Examiner has objected to the specification as being confusing for referring to two different Deposit Numbers. In response, Applicant has amended the specification to disclose the relationship between Deposit Number B-11474 (*Corynebacterium glutamicum*) and Deposit Number B-30293 (*E. coli*). As recited in the specification, the feedback resistant pyruvate carboxylase gene of the present invention was isolated and cloned from Deposit Number NRRL B-11474. The isolated/cloned pyruvate carboxylase gene was deposited in an *E. coli* host cell under Deposit Number NRRL B-30293. The *E. coli* deposit was made for ease of extraction and reproduction.

The Examiner is correct that the experimental data presented in the Tables and Figures refers to *C. glutamicum* NRRL B-11474 and not to *E. coli* NRRL B-30293. The reason for this is

simply that the experiments were performed on the pyruvate carboxylase gene contained in, and isolated from, the *C. glutamicum* host cell and not the *E. coli* host cell.

Accordingly, in view of the above and the amendment to the specification, Applicant respectfully submits that the Examiner's objections to the specification have been overcome and respectfully requests withdrawal thereof.

§112 Rejections - Claim 2

In the Final Office Action, the Examiner has rejected claim 2 under 35 USC § 112, first paragraph. The Examiner has indicated that the enablement requirement has been met by the deposit (Deposit Number B-30293) and Applicant's Viability Statement in the Amendment filed August 22, 2003. However, the Examiner has stated the specification still must contain a description of what the deposit contains.

In response, Applicant has amended the specification to contain a description of what Deposit Number B-30293 contains. The feedback resistant pyruvate carboxylase gene of the present invention was isolated and cloned from Deposit Number NRRL B-11474, and the isolated/cloned gene was deposited in an *E. coli* host cell under Deposit Number NRRL B-30293. The *E. coli* deposit (B-30293) was made for ease of extraction and reproduction. Applicant respectfully submits that no new matter has been added.

Accordingly, in view of the above and the amendment to the specification, Applicant respectfully submits that claim 2 is in allowable form and respectfully requests withdrawal of the Examiner's rejections.

§ 112 Rejections - Claims 1, 5-8 and 12-13

In the Final Office Action, the Examiner has rejected pending claims 1, 5-8 and 12-13 under 35 USC § 112, first paragraph. Applicant believes the main basis for the Examiner's § 112

rejections is that the number of allowed mutations recited in the pending claims is not limited in terms of the mutant's sequence homology to SEQ ID NO:1.

In response, Applicant has amended claim 1 to recite that the nucleic acid molecule claimed therein comprises a nucleotide sequence "at least 95% identical to SEQ ID NO:1" and which codes for a pyruvate carboxylase enzyme. Applicant believes that the amendment to claim 1 places it in allowable form, as the nucleic acid claimed therein is limited to the structure homologous to SEQ ID NO:1.

Applicant's amendment to claim 1 specifies a limit on the number of substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:1. Support for the amendment to claim 1 is found in various portions of the specification, including paragraphs [0016], [0017], [0018], [0020], [0021], [0043] and [0044] of the specification.

Claim 1, as amended, now limits the number of allowed mutations in terms of the mutant's sequence homology to SEQ ID NO:1. Thus, the scope of claims 1, 5-8 and 12-13 is commensurate with the enablement provided by the disclosure. Accordingly, Applicant submits that claims 1, 5-8 and 12-13 are in allowable form, and respectfully requests withdrawal of the Examiner's rejections.

§ 112 Rejections - Claims 19-20

In the Final Office Action, the Examiner has rejected pending claims 19-20 under 35 USC § 112, first paragraph. Applicant believes the main basis for the Examiner's § 112 rejections is that many functionally unrelated DNAs are encompassed within the scope of claims 19-20, including partial DNA sequences, while the specification discloses only a single species of the claim genus.

In response, Applicant has amended claim 19 to recite that the nucleic acid molecule claimed therein is "at least 95% identical to SEQ ID NO:1 and which codes for a pyruvate carboxylase enzyme desensitized to feedback inhibition by aspartic acid". Claim 19, as amended, limits the genus of DNAs that comprise the recited sequences to a pyruvate carboxylase enzyme having a known homology to SEQ ID NO:1. Additionally, claim 19 recites the functionality of the polypeptides comprising the recited fragments. Thus, the remainder of the structure of a polypeptide with the pyruvate carboxylase enzyme desensitized to feedback inhibition by aspartic acid has been defined.

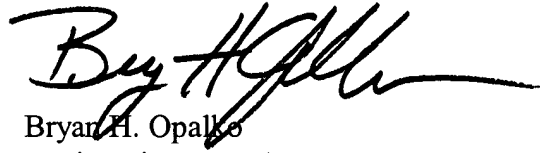
Claim 19, as amended, is now limited in terms of the requisite pyruvate carboxylase activity and homology to SEQ ID NO:1. Accordingly, Applicant submits that the scope of claims 19-20 is now commensurate with the enablement provided by the specification. Applicant submits that claims 19-20 are in allowable form, and respectfully requests withdrawal of the Examiner's rejections.

Conclusion

For at least the above-identified reasons, Applicant submits that claims 1-3, 5-8, 12-13 and 19-20 are in allowable form. Applicant believes the amendments made herein place the application in allowable form and respectfully request entry of said amendments. Reconsideration of pending claims 1-3, 5-8, 12-13 and 19-20, allowance and passage to issue are respectfully requested.

It is believed that this Amendment requires no fee above that included for the Request for Continued Examination. However, if an additional fee is required for any reason, the Commissioner is hereby authorized to charge Deposit Account No. 02-4553 the necessary amount.

Respectfully submitted,



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EFFECT OF VARIOUS SUBSTRATE CONCENTRATIONS ON PYRUVATE CARBOXYLASE ACTIVITY FROM *C. glutamicum* ~~BF100~~ (○) AND ATCC 21253 (●).

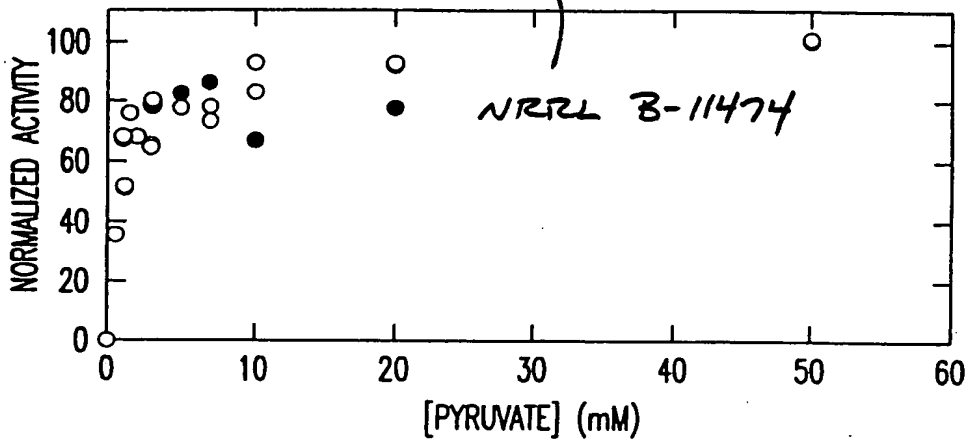


FIG. 3A

EFFECT OF VARIOUS SUBSTRATE CONCENTRATIONS ON PYRUVATE CARBOXYLASE ACTIVITY FROM *C. glutamicum* ~~BF100~~ (○) AND ATCC 21253 (●).

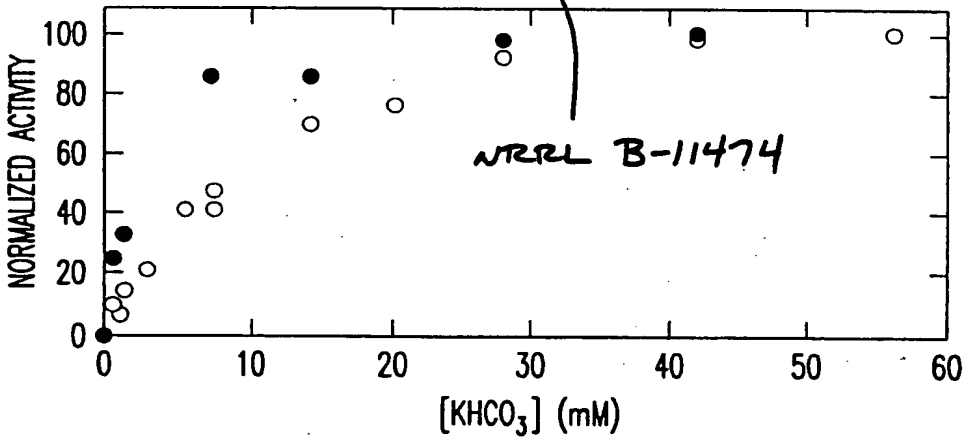


FIG. 3B

EFFECT OF VARIOUS SUBSTRATE CONCENTRATIONS ON PYRUVATE CARBOXYLASE ACTIVITY FROM *C. glutamicum* ~~BF100~~ (○) AND ATCC 21253 (●).

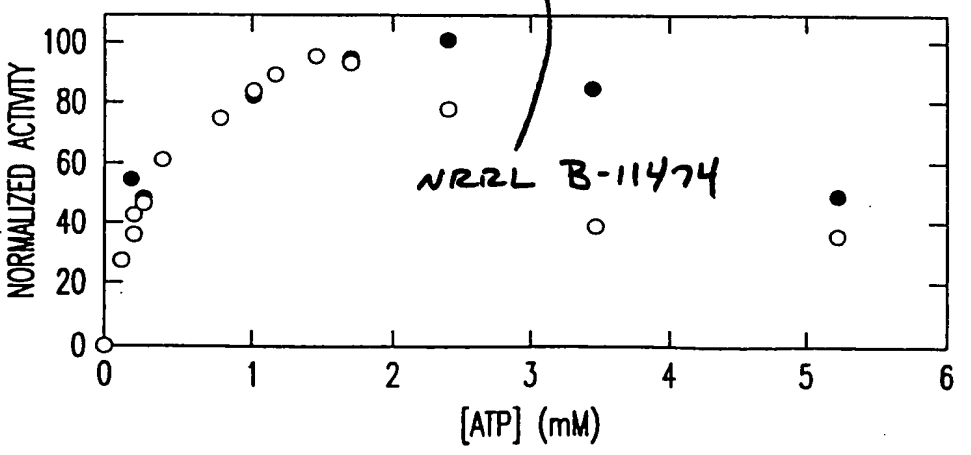


FIG. 3C

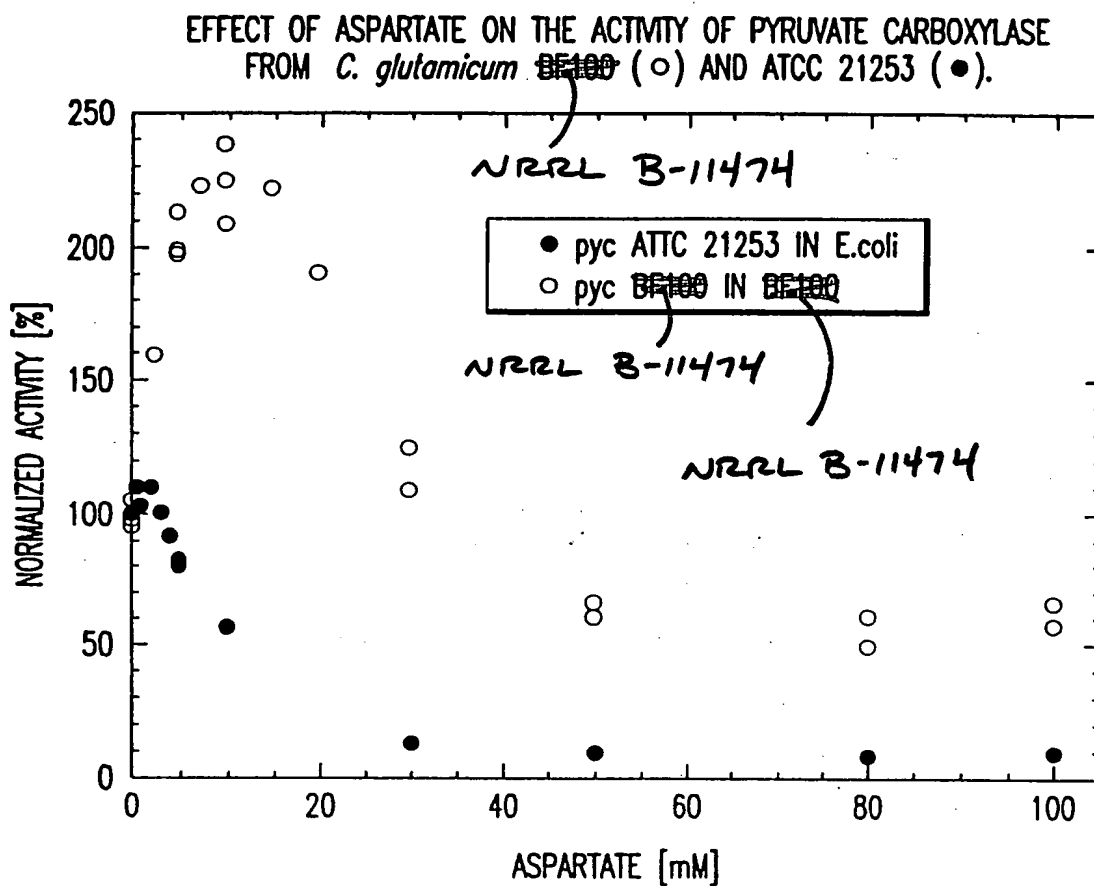


FIG. 4



EFFECT OF Acetyl-CoA ON PYRUVATE CARBOXYLASE ACTIVITY FROM
C. glutamicum NRRL B-11474 (○) AND ATCC 21253 (●).

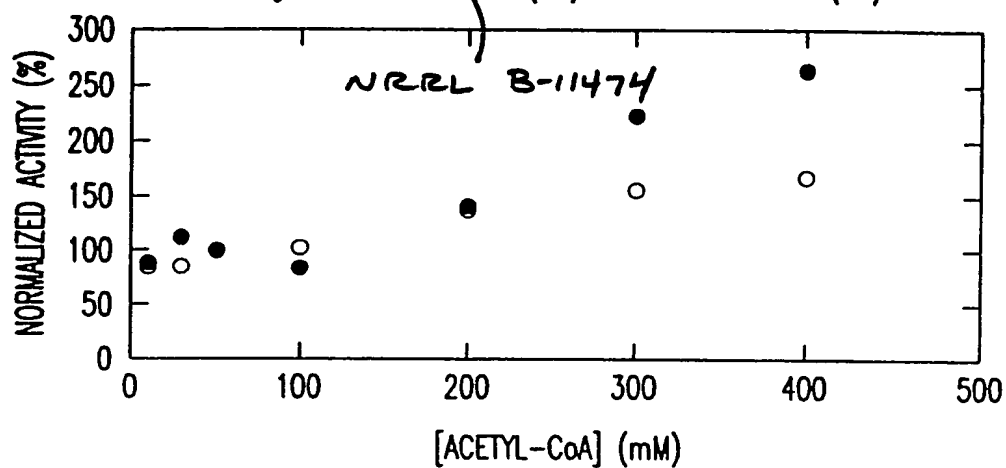


FIG. 5